Pooled genome-wide analysis of kidney cancer risk

Renal cell carcinoma (RCC) is the 8th most common cancer in the US and the 10th most common form of cancer death, with a particularly high incidence among African Americans. A sharp increase in the incidence of RCC was observed in recent decades with some of the greatest increases happening in Central Europe and among the black population in the US. Apart from smoking, obesity and hypertension, much of the etiology of this disease remains to be identified. There is increasing evidence that genetic factors influence susceptibility to RCC, although this hypothesis has been understudied.

We have recently completed a genome-wide association study (GWAS) of RCC comprising 3,800 cases and 8,500 controls. We now propose to extend this study by incorporating an additional 4,000 cases and 5,000 controls from a series of population based case-control and cohort studies. Inclusion of cohort studies has been facilitated via the NCI cohort consortium initiative. In addition to its size, our study will be unique in several ways: (1) extensive clinicopathological information and survival of cases will be collected; (2) genome-wide analyses for the association between genetic variants and RCC will be conducted for the disease onset and survival in parallel; (3) a comprehensive biorepository of germline DNA and tumor DNA and RNA on at least 2,000 cases will be developed; (4) whole-genome gene expression profiling on fresh renal tissue and tumor tissue will be obtained to complement results obtained from the germline genotyping analyses.

PUBLIC HEALTH RELEVANCE: The incidence of kidney cancer has been increasing over the past decades and the disease has a very poor prognosis when diagnosed at an advanced stage (20% of the cases in the US). Apart from smoking, obesity and hypertension, much of the etiology of this disease remains to be identified. We propose to investigate genetic factors associated with kidney cancer onset and survival, looking at the genetic variants across the whole genome, and combining this with gene expression analysis of the tumor tissue.

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